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Patent Department (TR-E)		
Case	21810	Int.-Nr.
Literatur crfcast:	Zeichen:	Datum:
Lit.sheet	Endnote	SOA
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Roche Diagnostics GmbH Patent Department (TR-E) Penzberg					
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Datum/Date
04.02.04

Zeichen/Ref./Réf. 21810 EP-HIL	Anmeldung Nr./Application No./Demande n°/Patent Nr./Patent No./Brevet n°. 03014929.8-2402-
Anmelder/Applicant/Demandeur/Patentinhaber/Proprietor/Titulaire Roche Diagnostics GmbH, et al	

COMMUNICATION

The European Patent Office herewith transmits as an enclosure the European search report for the above-mentioned European patent application.

If applicable, copies of the documents cited in the European search report are attached.

☒ Additional set(s) of copies of the documents cited in the European search report is (are) enclosed as well.

The following specifications given by the applicant have been approved by the Search Division:

☒ abstract ☒ title

☐ The abstract was modified by the Search Division and the definitive text is attached to this communication.

The following figure will be published together with the abstract: NONE

REFUND OF THE SEARCH FEE

If applicable under Article 10 Rules relating to fees, a separate communication from the Receiving Section on the refund of the search fee will be sent later.





European Patent
Office

PARTIAL EUROPEAN SEARCH REPORT

Application Number

which under Rule 45 of the European Patent Convention shall be considered, for the purposes of subsequent proceedings, as the European search report

EP 03 01 4929

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
✓ X Y	US 6 150 107 A (MATHIES RICHARD A ET AL) 21 November 2000 (2000-11-21) * abstract * * column 2, line 1 - column 2, line 28 * * examples 1-5 * * claims 1-28 * ---	1-6,8,9 7,10,12	C12Q1/68
✓ X Y	US 6 177 247 B1 (JU JINGYUE ET AL) 23 January 2001 (2001-01-23) * abstract * * column 2, line 11 - column 2, line 34 * * column 3, line 46 - column 4, line 16 * * column 5, line 32 - column 5, line 45 * * column 6, line 13 - column 6, line 22 * * column 7, line 18 - column 7, line 21 * * example I * * claims 1-45 * --- -/--	1-6,8,9 7,10,12	TECHNICAL FIELDS SEARCHED (Int.Cl.7) C12Q
INCOMPLETE SEARCH			
<p>The Search Division considers that the present application, or one or more of its claims, does/do not comply with the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for these claims.</p> <p>Claims searched completely :</p> <p>Claims searched incompletely :</p> <p>Claims not searched :</p> <p>---</p> <p>Reason for the limitation of the search:</p> <p>Since the application does not contain a claim 11, the search was limited to the present claims 1-10 and 12.</p>			
Place of search MUNICH		Date of completion of the search 9 December 2003	Examiner Madlener, M
CATEGORY OF CITED DOCUMENTS			
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons ----- & : member of the same patent family, corresponding document	

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EPO FORM 1503 03.02 (P04C07)



DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
✓ X	US 5 869 255 A (JU JINGYUE ET AL) 9 February 1999 (1999-02-09)	1-6,8,9	
Y	* abstract * * claims 1-20 * * figures 1,3 *	7,10,12	
✓ X	--- VET J A M ET AL: "Multiplex detection of four pathogenic retroviruses using molecular beacons" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 96, 1999, pages 6394-6399, XP002145609 ISSN: 0027-8424	1-6,8,9	
Y	* abstract * * page 6399, left-hand column * * figures 1,2 *	7,10,12	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
✓ X	--- JU J ET AL: "DESIGN AND SYNTHESIS OF FLUORESCENCE ENERGY TRANSFER DYE-LABELED PRIMERS AND THEIR APPLICATION FOR DNA SEQUENCING AND ANALYSIS" ANALYTICAL BIOCHEMISTRY, ACADEMIC PRESS, SAN DIEGO, CA, US, vol. 231, no. 1, 10 October 1995 (1995-10-10), pages 131-140, XP000536518 ISSN: 0003-2697	1-6,8,9	
Y	* abstract * * figures 1,3 *	7,10,12	
	--- -/--		



DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
✓ D,Y	US 6 369 893 B1 (CHANG RONALD ET AL) 9 April 2002 (2002-04-09) * abstract * * column 3, line 41 - column 5, line 42 * ---	1-10,12	
✓ D,Y	WO 97 46714 A (RASMUSSEN RANDY P ;UNIV UTAH RES FOUND (US); RIRIE KIRK M (US); WI) 11 December 1997 (1997-12-11) * abstract * * page 4, paragraph 3 - page 22, paragraph 3 * * examples 5-9 * * claims 1-126 * ---	1-10,12	
✓ D,Y	US 6 197 520 B1 (BERNARD PHILIP ET AL) 6 March 2001 (2001-03-06) * the whole document * ---	1-10,12	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
✓ Y	US 6 140 054 A (WITTWER CARL T ET AL) 31 October 2000 (2000-10-31) * abstract * * column 12, line 57 - column 13, line 7 * ---	1-10,12	
✓ D,Y	"Rotor-Gene 3000 Four-Channel Multiplexing System", CORBETT RESEARCH , INTERNET (CORBETT RESEARCH HOMEPAGE) XP002264359 * the whole document * ---	1-10,12	
✓ D,A	MATTHEWS J A ET AL: "ANALYTICAL STRATEGIES FOR THE USE OF DNA PROBES" ANALYTICAL BIOCHEMISTRY, ORLANDO, FL, US, vol. 169, no. 1, 15 February 1988 (1988-02-15), pages 1-25, XP000670180 ISSN: 0003-2697 * the whole document, in particular p. 18, left column and Fig. 11 * --- -/--	1-10,12	



DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.CI.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
✓ A	GLAZER ALEXANDER N ET AL: "Energy-transfer fluorescent reagents for DNA analyses" CURRENT OPINION IN BIOTECHNOLOGY, vol. 8, no. 1, 1997, pages 94-102, XP002264350 ISSN: 0958-1669 * the whole document *	1-10,12	
✓ A	HEID C A ET AL: "REAL TIME QUANTITATIVE PCR" GENOME RESEARCH, COLD SPRING HARBOR LABORATORY PRESS, US, vol. 6, no. 10, 1 October 1996 (1996-10-01), pages 986-994, XP000642795 ISSN: 1088-9051 * the whole document *	1-12	
			TECHNICAL FIELDS SEARCHED (Int.CI.7)

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

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This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
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09-12-2003

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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

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**ANNEX TO THE EUROPEAN SEARCH REPORT
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US 6140054	A	31-10-2000	AU 6280599 A	17-04-2000
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			WO 0018965 A1	06-04-2000
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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82



This application is covered by the extended European search report pilot project at present running within the European Patent Office, applied to all European patent applications filed : first filing and searched on or after 01.07.03. Under this project the EPO issues together with the search report an opinion on whether the application and the invention to which it relates meet the requirements of the EPC. This non-binding opinion is issued free of charge as a service. This opinion may be used as the basis for an informed decision as to whether it is desired to pursue the application further or not.

For further details of this pilot project, the applicant's attention is directed to the Official Journal edition 5/2003. If any further immediate questions or comments arise the EPO Customer Services: +31-70-340 4500 or +49-89-2399 2828 can be contacted.

The attached opinion reveals that the application or the invention to which it relates appear not to meet the requirements of the Convention (see comments on enclosed Form 2906).

If the applicant wishes to continue with this application the examination fee must be paid. Where appropriate amendments can be filed to address the objections raised in the opinion thus shortening the overall procedure. If no amendments are filed, the opinion will be re-issued as the first official communication under Article 96(2) and Rule 51(2) EPC.

If the examination fee has already been paid and the right to the communication under Article 96(1) EPC has been waived for this application, the first official communication under Article 96(2) and Rule 51(2) EPC will be issued promptly.



The examination is being carried out on the **following application documents**:

Text for the Contracting States:

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PT RO SE SI SK TR LI

Description, pages:

1-35 as originally filed

Claims, No.:

1-12 as originally filed

Drawings, sheets:

1/15-15/15 as originally filed

1. The following documents are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

D1: US 6,150,107 (November 21, 2000)
D2: US 6,177,247 (January 23, 2001)
D3: Ju J et al. (1995), Anal. Biochem., Vol. 231, pp. 131-140
D4: US 5,869,255 (Feb. 9, 1999)
D5: Matthews JA et al. (1988), Anal. Biochem., Vol. 169, pp. 1-25
D6: WO 97/46714 (December 11, 1997)
D7: US 6,197,520 (March 6, 2001)
D8: Corbett Research: "Rotor-Gene 3000" (internet print-out)
D9: WO 98/49340 (November 5, 1998)
D10: US 6,369,893 (April 9, 2002)
D11: Vet JAM et al. (1999), Proc. Natl. Acad. Sci., Vol. 96, pp. 6394-6399

2. In view of this prior art, the present claims 1-12 do not meet the requirements of the EPC for the following reasons.



3. Lack of novelty (Articles 52(1), 54(1) and (2) EPC)

3.1 It is noted that **claim 1** relating to "a composition or reaction mixture for performing..." has to be construed as meaning merely "a composition or reaction mixture suitable for performing..." (cf. Guidelines, Part C, Chapter III, section 4.8).

3.2a **D1** discloses a composition comprising 3 FRET hybridization probes, each probe comprising a FRET donor moiety and a FRET acceptor moiety having an emission maximum between 550 and 710 nm (cf., e.g., D1, Examples 1-5; Fig. 4; D2, abstract; Fig. 3) as well as its use in PCR (cf., e.g., D1, col. 6, l. 55 - col. 7, l. 34). D1 also explicitly discloses that "[p]rocedures depending on fragment labeling by ligation are performed in an analogous manner" (D1, col. 7, ll. 33-34), i.e., procedures utilizing primer pairs (cf., e.g., D5, p. 18, left col.; Fig. 11). Hence, D1 is considered to destroy the novelty of **claim 1** (Articles 52(1), 54(1) and (2) EPC).

3.2b **D1** furthermore discloses the use of R6G and/or TAMRA as FRET acceptor moiety (cf., e.g., D1, col. 4, ll. 20-36). Thus, **claim 6** likewise lacks novelty over **D1** (Articles 52(1) and 54(1) and (2) EPC).

3.2c Given the fact that **D1** discloses ligation-dependent multi-color PCR processes using four FRET acceptor/donor pairs (cf. the above-cited passages), D1 is also considered to anticipate the subject-matter of **claims 8-9** pursuant to Articles 52(1), 54(1) and (2) EPC.

3.3 Analogous objections with regard to **claims 1, 6, 8 and 9** result from the disclosure of **D2** (cf., e.g., D2, abstract; col. 2, ll. 11-34; col. 3, l. 46 - col. 4, l. 16; col. 5, ll. 32-45; col. 6, ll. 13-22; col. 7, ll. 18-21; claims 1-45; Ex. I). Hence, said claims are considered to lack novelty over D2 (Articles 52(1), 54(1) and (2) EPC).

4. Lack of inventive step (Articles 52(1) and 56 EPC)

4.1 Given the fact that the simultaneous use of at least four FRET donor-acceptor-pairs was known prior to the priority date of the present application (cf., e.g., the above-cited passages of **D1** and **D2**; cf. also the teaching provided in **D11**, in particularly p. 6399, left col.), that the prior art teaches how far the individual



emission maxima should suitably lie apart (cf., e.g., **D1**, col. 4, ll. 37-45), that there existed a wide variety of commercially available fluorophors prior to the effective date of the present application (**D1**, col. 4, ll. 20-36), and that **D3 and D4** both individually disclose the use of 4 FRET fluorescein donors (cf., e.g., **D3**, abstract; **D4**, Fig. 1), the additional features of dependent **claims 2-5** would not appear suitable to establish the inventive step required by Article 56 EPC.

4.2 In view of the fact that the use of the compositions of claim 1 for PCR is disclosed in **D1/D2** (cf. section 3.2-3.3, *supra*) and that real time PCR instruments suitable for the purpose defined in claim 7 formed part of the prior art (cf., e.g., **D6-D10**), the "system" according to **claim 7** is considered to lack the inventive step required by Art. 56 EPC. It is noted that the Applicant acknowledges the suitability of these prior art devices for the process of interest (cf. page 2, line 5 - page 4, line 16).

4.3 In view of the above (cf. sections 3.1-4.1, *supra*), the subject-matter of **claims 10 and 12** would also appear to lack the inventive step required by Article 56 EPC.

5. Lack of clarity (Article 84 EPC)

5.1 The term "system" in **claim 7** renders its category unclear (Article 84 EPC).

5.2 The numbering of the claims seems to be erroneous (the claim following claim 7 has no number; no claim 11). Thus, the set of claims as a whole would appear to lack clarity and hence to violate Article 84 EPC.

6. Concluding remarks

- (a) It is not at present apparent which part of the application could serve as a basis for a new, allowable claim. Should the applicant nevertheless regard some particular matter as patentable, an independent claim should be filed taking account of Rule 29(1) EPC. The applicant should also indicate in the letter of reply the difference of the subject-matter of the new claim vis-à-vis the state of the art and the significance thereof.
- (b) If the Applicant thinks that all of the objections raised above are overcome, then



the description should, at the same time, be brought into conformity with the amended claims. Care should be taken during revision not to add subject-matter which extends beyond the content of the application as originally filed (Article 123(2) EPC). Any statements of problem or advantage should be restricted to the letter of reply.

- (c) The amendments should be filed by way of replacement pages, avoiding unnecessary recasting of the description. The Applicant should also take account of the requirements of Rule 36(1) EPC. If handwritten amendments are submitted, they should be clearly legible for the printer.
- (d) In the reply, the parts of the application, as originally filed, which form the basis for the amendments (cf. Article 123(2) EPC) should be clearly indicated.
- (e) In order to expedite the procedure, the Applicant is kindly asked to clearly point out where the amendments have been made, possibly by enclosing a copy of the original pages with the corrections in manuscript.
- (f) Independently of the above objections, it is further noted that a European patent application should be self-contained. Therefore, references to prior art documents as "being incorporated by reference", e.g., page 3, line 15, should be deleted (cf. Guidelines, C-II, 4.18).

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